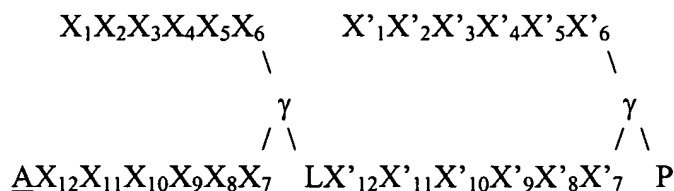


Claim 23. (Amended) A tandem-linked polyamide having the formula:



wherein  $\gamma$  is  $-\text{NH}-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CONH}-$  hairpin linkage derived from  $\gamma$ -aminobutyric acid or a chiral hairpin linkage derived from 2,4-diaminobutyric acid;

$X_1/X_{12}$ ,  $X_2/X_{11}$ ,  $X_3/X_{10}$ ,  $X_4/X_9$ ,  $X_5/X_8$ ,  $X_6/X_7$ ,  $X'_1/X'_{12}$ ,  $X'_2/X'_{11}$ ,  $X'_3/X'_{10}$ ,  $X'_4/X'_9$ ,  $X'_5/X'_8$ , and  $X'_6/X'_7$  represent carboxamide binding pairs which bind DNA base pairs and are selected from the group consisting of Hp/Py, Py/Hp, Py/Im, Im/Py, and Py/Py to correspond to the DNA base pair in the minor groove to be bound;

L represents an amino acid linking group selected from the group consisting of  $\beta$ -alanine and 5-aminovaleric acid ( $\delta$ );

P represents a polyamide selected from the group consisting of  $X_1X_2X_3\gamma X_4X_5X_6$ ,  $X_1X_2X_3X_4\gamma X_5X_6X_7X_8$ ,  $X_1X_2X_3X_4X_5\gamma X_6X_7X_8X_9X_{10}$ , and  $X_1X_2X_3X_4X_5X_6\gamma X_7X_8X_9X_{10}X_{11}X_{12}$ , where  $X_1-X_{12}$  are independently selected from the group consisting of  $\beta$ -alanine, pyrrole, hydroxypyrrole and imidazole; and

A represents a positive patch consisting of a rigid group adjacent to a positively charged group [such that a positive charge is delivered to the phosphate backbone or the major groove of a DNA molecule].

## REMARKS

The invention relates in part to polyamide molecules comprising one or more amino acids containing N-methylpyrrole, 3-hydroxy-N-methylpyrrole, or N-methylimidazole moieties, and a positive patch consisting of a rigid group adjacent to a positively charged group. Such molecules can provide sequence-specific binding within the minor groove of a DNA molecule, while

presenting the positively charged group in an orientation that allows the polyamide molecule to disrupt interactions between proteins and the phosphate backbone or major groove of the DNA molecule.

Claims 1-26 are pending in the instant application. Applicants have amended claims 1, 2, 6, 12, 14, 16, 18, and 20-23 herein. The amendments to the claims are fully supported by the specification, and do not add new matter or require a new search. Polyamides comprising one or more non- -amino acids containing N-methylpyrrole, 3-hydroxy-N-methylpyrrole, and N-methylimidazole moieties are described throughout the specification, e.g., on page 12, lines 21-28, and figures 1, 2, 4, 5, 7, 10, and 12. The additional amendments to the claims merely clarify the claimed subject matter using preferred language, and are not intended in any way to limit the scope of the claims.

Notwithstanding the foregoing, Applicants expressly reserve the right to pursue subject matter no longer or not yet claimed in one or more applications that may claim priority hereto. Applicants respectfully request reconsideration of the claims in view of the foregoing claim amendments and the following remarks.

*Non Art-Related Remarks*

Sequence Information

The Examiner states that the application fails to comply with the requirements set forth in 37 C.F.R. §§ 1.821 through 1.825. Specifically, the Examiner states that the amino acid sequence "RPRRRR" must be listed on the sequence listing, and that a paper copy must be provided. Paper No. 5, paragraph 1. Applicants respectfully submit that such a sequence listing was provided on October 18, 1999. A copy of Applicants' submission, including the paper copy of the sequence listing, is attached hereto as Appendix 1. Applicants note, in particular, that sequence number 7 consists of the amino acid sequence "Arg Pro Arg Arg Arg Arg," corresponding to the single letter amino acid abbreviation RPRRRR. Applicants, therefore, request that the Examiner withdraw this objection.

Drawings

Applicants note the objections of the Draftsperson to the drawings filed with the application, and will provide corrected drawings prior to issuance of the application as a patent.

35 U.S.C. § 112, Second Paragraph

The Examiner has rejected several claims as being allegedly vague: claim 1 and its dependent claims for the preamble to claim 1; claims 20-23 for allegedly failing to fully describe the abbreviations “Hp,” “Py,” and “Im;” claim 24 for its reference to claim 1; and claims 2, 5-6, and 22-23 for the phrase “and derivative thereof.” Applicants respectfully submit that the foregoing claim amendments render these rejections moot.

The Examiner has also rejected claims 2, 5, 6, 22, and 23, as allegedly containing an improper Markush format. Applicants respectfully disagree. The Markush groups in each of these claims are in the acceptable “selected from the group consisting of A, B, C... and Z.” Applicants request a clarification of the Examiner’s objection to this language.

The Examiner has also rejected claim 11, contending that the phrase “the R-2 amino group” lacks antecedent basis. Applicants respectfully traverse this rejection. Claim 11 is dependent upon claim 10, which recites “an (R)-2,4-diaminobutyric acid hairpin turn.” The skilled artisan will understand that a molecule designated as “(R)-2,4-diamino” inherently has both an R-2 amino group and an R-4 amino group. Inherent components of elements recited have antecedent basis in recitation of the element itself. See MPEP § 2173.05(e). Therefore, Applicants respectfully submit that the language objected to by the Examiner meets the standard of 35 U.S.C. § 112, second paragraph, and request that the Examiner withdraw the rejection.

Art-Related Remarks

The Examiner has rejected claims 1-8, 25, and 26 under 35 U.S.C §102 as allegedly being anticipated by Feng et al., Science 263: 348-355. Applicants respectfully traverse this rejection.

In order to anticipate a claim, a single prior art reference must provide each and every element set forth in the claim. Furthermore, the claims must be interpreted in light of the teachings of the specification. In re Bond, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). See also MPEP § 2131.

The instant claims, as amended herein, describe polyamides comprising one or more non- $\alpha$ -amino acids containing N-methylpyrrole, 3-hydroxy-N-methylpyrrole, or N-methylimidazole. As described in the instant specification, such polyamides can exhibit sequence-specific binding to the minor groove of a DNA molecule. See, e.g., specification, page 13, lines 1-4. In contrast, the Feng et al. reference discloses Hin recombinase, a polypeptide which binds to DNA through the interaction of DNA binding regions comprising only  $\alpha$ -amino acids such as glycine, arginine, proline, isoleucine, lysine, methionine, and asparagine. See, e.g., Feng et al., pages 351-352. Thus, the Feng et al. reference does not disclose any polyamides comprising one or more non- $\alpha$ -amino acids containing N-methylpyrrole, 3-hydroxy-N-methylpyrrole, or N-methylimidazole, as required by the instant claims.

Accordingly, because the Feng et al. reference fails to disclose the instantly claimed polyamide molecules, the instant claims are not anticipated by Feng et al. Applicants, therefore, request that the rejection under 35 U.S.C. § 102 be withdrawn.

The Examiner has also rejected claims 1, 5, 9, 25, and 26 under 35 U.S.C §102 as allegedly being anticipated by Bruice et al., Proc. Nat'l. Acad. Sci. USA 89:1700-1704. Applicants respectfully traverse this rejection.

The instant claims describe polyamide molecules that comprise, amongst other elements, a positive patch consisting of a rigid group adjacent to a positively charged group. Rigid groups are described in the instant specification, e.g., on page 17, line 16, through page 18, line 11. The rigid group advantageously "positions the positively charged group such that contact with the major groove or the phosphate backbone of a DNA molecule is accomplished." Id., page 17, lines 17-18.

In contrast, the Bruice et al. reference does not disclose any polyamides that comprise a positive patch comprising a rigid group adjacent to a positively charged group, as required in the instant claims. Moreover, the Examiner has not addressed this element of the instantly claimed invention, instead simply stating that the polyamides of the Bruice et al. reference show minor groove binding associated with "interaction of the positively charged polyamide side chain with phosphodiester linkages." Paper No. 5, paragraph 14. Thus, no prima facie case of anticipation has been demonstrated.

Accordingly, because the Bruice et al. reference fails to disclose any polyamide molecules comprising a positive patch consisting of a rigid group adjacent to a positively charged group, the instant claims are not anticipated by Bruice et al. Applicants, therefore, request that the rejection under 35 U.S.C. § 102 be withdrawn.


#### CONCLUSION

Applicants respectfully submit that the pending claims are in condition for allowance. An early notice to that effect is earnestly solicited. Should any matters remain outstanding, the Examiner is encouraged to contact the undersigned at the address and telephone number listed below so that they may be resolved without the need for additional action and response thereto.

Respectfully submitted,

BROBECK, PHLEGER & HARRISON LLP

Dated: December 29, 2000

By:   
Michael A. Whittaker  
Registration No. 46,230

Brobeck, Phleger & Harrison LLP  
12390 El Camino Real  
San Diego, CA 92130  
Telephone: (858) 720-2500  
Facsimile: (858) 720-2555